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REMARKS

With this amendment, the limitations of claims 19-21 are incorporated into claim 18. No new matter is added. Claim 18 remains pending in this application.

Rejection under 35 U.S.C. § 103(a)

Claims 18-21 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Critchley (2002), Buck, et al. (1999), and Mackay, et al. (2002) as evidenced by Froguel, et al. (1993) and Howell, et al. (1999).

The Examiner states that Critchley teaches the mitochondrial DNA 3243 mutation in sequence 13. As per the previous response, the 480 base pair segment referenced of Critchley (SEQ ID NO: 13) is merely a segment of the human mitochondrion complete genome which includes the A3243G mutation which is not a probe and does not correspond to the probes claimed by Applicants because it is 462-464 base pairs longer than the probes of Applicant's claimed method.

Froguel, et al. and Howell, et al. are relied upon for teaching methods of detecting mutations. Froguel merely teaches PCR methods

Regarding Howell, et al., as shown in Fig.1 and described in Method principle of Howell, a target sequence is amplified by PCR and then the probe target strand is isolated. After that, probes and intercalating dye are added.

On the other hand, as described in Example 2 and page 20, third paragraph of the present specification, probes are added <u>before</u> PCR in the method of the presently claimed invention. Further, even if the probes could be used in the DASH method, there is low possibility that they can also be used in the method of the present invention. Thus, it was difficult to design suitable probes in the present application.

Therefore, even if the DASH method of Howell is combined with Critchley, the method of the present invention cannot be obtained. The combination of references does not lead one of ordinary skill in the art to the claimed invention.

Further, the method of the present invention has unexpected effects as follows.

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In the method of the present invention, it is not necessary to isolate the probe target strand, unlike the DASH method. Therefore, the method of the present invention can be performed more quickly.

As described in page 20, third paragraph and Industrial Applicability of the present specification, only Tm of the probe is analyzed after amplification of a nucleic acid, and therefore it is not necessary to handle the amplification product after completion of the reaction. Thus, there is no risk of contamination with the amplification product.

As described above, except for difficulties in designing the probes, there are many advantage of the claimed method compared with the DASH method.

As previously argued, among many probes for detecting the mitochondrial DNA 3243 mutation, a nucleic acid probe wherein the 3' end of the probe is a cytosine corresponding to the nucleotide number 230 of SEQ ID NO:2 is important. Specifically, as shown in Figure 5, the probes of the present invention (i.e. SEQ ID NOS:21 and 22) were able to detect the mitochondrial DNA 3243 mutation. However, as shown in Figure 4, probes other than the probes of the present invention were not able to detect the mitochondrial DNA 3243 mutation.

The importance of the nucleotide number 230 was discovered by the Applicant through trial and error process and thus the probes of the present invention were not easily obtained by one of ordinal skill in the art based on the descriptions of the cited references.

In view of Applicant's amendments and arguments, reconsideration and withdrawal of the above ground of rejection is respectfully requested.

Information Disclosure Statement

References previously submitted on February 16, 2009 are resubmitted herewith. Applicant has obtained better copies of these references.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather,

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any alterations or characterizations are being made to facilitate expeditious prosecution of this

application. Applicant reserves the right to pursue at a later date any previously pending or other

broader or narrower claims that capture any subject matter supported by the present disclosure,

including subject matter found to be specifically disclaimed herein or by any prior prosecution.

Accordingly, reviewers of this or any parent, child or related prosecution history shall not

reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter

supported by the present application.

CONCLUSION

In view of Applicants' amendments to the claims and the foregoing Remarks, it is

respectfully submitted that the present application is in condition for allowance. Should the

Examiner have any remaining concerns which might prevent the prompt allowance of the

application, the Examiner is respectfully invited to contact the undersigned at the telephone

number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or

credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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